

WHAT IS CLAIMED

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

5 (a) the nucleotide sequence as set forth in SEQ ID NO:1 or SEQ ID NO:3;

(b) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

10 (c) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of (a) or (b), wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4; and

15 (d) a nucleotide sequence complementary to any of (a)-(c).

2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

20 (a) a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4, wherein the 25 polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO:1 or SEQ ID NO:3, wherein

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the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(c) a nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3; (a) or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(d) a nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or (a)-(c) comprising a fragment of at least about 16 nucleotides;

(e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(d), wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4; and

(f) a nucleotide sequence complementary to any of (a)-(c).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at

PCT/US2002/024980

least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(c) a nucleotide sequence encoding a polypeptide  
5 as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(d) a nucleotide sequence encoding a polypeptide  
10 as set forth in SEQ ID NO:2 or SEQ ID NO:4 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(e) a nucleotide sequence encoding a polypeptide  
15 as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the  
20 polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(f) a nucleotide sequence of (a)-(e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under  
25 moderately or highly stringent conditions to the complement of any of (a)-(f), wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4; and

(h) a nucleotide sequence complementary to any of  
30 (a)-(e).

*SAC* 4. A vector comprising the nucleic acid molecule  
of Claims 1, 2, or 3.

5 5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic  
cell.

10 7. The host cell of Claim 5 that is a prokaryotic  
cell.

15 8. A process of producing a Cloaked-2 polypeptide  
comprising culturing the host cell of Claim 5 under  
suitable conditions to express the polypeptide, and  
optionally isolating the polypeptide from the culture.

20 9. A polypeptide produced by the process of  
Claim 8.

25 10. The process of Claim 8, wherein the nucleic  
acid molecule comprises promoter DNA other than the  
promoter DNA for the native Cloaked-2 polypeptide  
operatively linked to the DNA encoding the Cloaked-2  
polypeptide.

30 11. The isolated nucleic acid molecule according  
to Claim 2 wherein the percent identity is determined  
using a computer program selected from the group  
consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA,  
BLASTX, BestFit, and the Smith-Waterman algorithm.

*Seq 02* > 12. A process for determining whether a compound  
inhibits Cloaked-2 polypeptide activity or production  
comprising exposing a cell according to Claims 5, 6,  
5 or 7 to the compound, and measuring Cloaked-2  
polypeptide activity or production in said host cell.

10 13. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:4.

14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

15 (a) the mature amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4, optionally further comprising an amino-terminal methionine;

20 (b) an amino acid sequence for an ortholog of SEQ ID NO:2 or SEQ ID NO:4, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

25 (c) an amino acid sequence that is at least about 70, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

30 (d) a fragment of the amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:4 comprising at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;

(e) an amino acid sequence for an allelic variant or splice variant of either the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4, or at least one of (a)-(c) wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4.

15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

- 10 (a) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;
- 15 (b) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;
- 20 (c) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4;
- 25 (d) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4; and

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(e) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4, with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO:2 or SEQ ID NO:4.

10        16. A polypeptide according to claim 14 or 15 wherein the amino acid at position 9 of SEQ ID NO: 2 is aspartic acid or glutamic acid.

15        17. A polypeptide according to claim 14 or 15 wherein the amino acid at position 39 of SEQ ID NO: 2 is glycine, proline, or alanine.

20        18. A polypeptide according to claim 14 or 15 wherein the amino acid at position 58 of SEQ ID NO: 2 is arginine, lysine, glutamine, or asparagine.

25        19. A polypeptide according to claim 14 or 15 wherein the amino acid at position 81 of SEQ ID NO: 2 is valine, isoleucine, methionine, leucine, phenylalanine, alanine, or norleucine.

20. A polypeptide according to claim 14 or 15 wherein the amino acid at position 102 of SEQ ID NO: 2 is tryptophan, tyrosine, or phenylalanine.

21. A polypeptide according to claim 14 or 15 wherein the amino acid at position 154 of SEQ ID NO: 2 is serine, threonine, or alanine.

*5 203 >* 22. An isolated polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3.

10 23. The isolated polypeptide according to Claim 14 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

15 24. An antibody produced by immunizing an animal with a peptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

*Subcut* 25. An antibody or fragment thereof that specifically binds the polypeptide of Claims 13, 14, 20 or 15.

26. The antibody of Claim 25 that is a monoclonal antibody.

.25 27. A hybridoma that produces a monoclonal antibody that binds to a peptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

*205 > 30* 28. A method of detecting or quantitating the amount of Cloaked-2 polypeptide using the anti-Cloaked-2 antibody or fragment of Claims 24, 25, or 26.

29. A selective binding agent or fragment thereof  
that specifically binds at least one polypeptide  
wherein said polypeptide comprises the amino acid  
5 sequence selected from the group consisting of:

- a) the amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4; and
- 10 b) a fragment of the amino acid sequence set forth in at least one of SEQ ID NO:2 or SEQ ID NO:4; and
- c) a naturally occurring variant of (a) or (b).

30. The selective binding agent of Claim 29 that  
is an antibody or a fragment thereof.

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31. The selective binding agent of Claim 29 that  
is a humanized antibody.

32. The selective binding agent of Claim 29 that  
20 is a human antibody or a fragment thereof.

33. The selective binding agent of Claim 29 that  
is a polyclonal antibody or a fragment thereof.

25 34. The selective binding agent of Claim 29 that  
is a monoclonal antibody or a fragment thereof.

35. The selective binding agent of Claim 29 that  
is a chimeric antibody or a fragment thereof.

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36. The selective binding agent of Claim 29 that is a CDR-grafted antibody or a fragment thereof.

~~37. The selective binding agent of Claim 29 that 5 is an antiidiotypic antibody or a fragment thereof.~~

38. The selective binding agent of Claim 29 which is a variable region fragment.

10 39. The variable region fragment of Claim 38 which is a Fab or a Fab' fragment.

15 40. A selective binding agent or fragment thereof comprising at least one complementarity-determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

41. The selective binding agent of Claim 29 which is bound to a detectable label.

20 42. The selective binding agent of Claim 29 which antagonizes Cloaked-2 polypeptide biological activity.

25 43. A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 29.

30 44. A selective binding agent produced by immunizing an animal with a polypeptide comprising an

amino acid sequence selected from the group consisting of SEQ ID NO:2 or SEQ ID NO:4.

*Suga 6* 45. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to Claims 1, 2, or 3.

46. A composition comprising the polypeptide of Claims 13, 14, or 15 and a pharmaceutically acceptable formulation agent.

47. The composition of Claim 46 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

48. The composition of Claim 46 wherein the polypeptide comprises the mature amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4.

*Suga 7* 49. A polypeptide comprising a derivative of the polypeptide of Claims 13, 14, or 15.

50. The polypeptide of Claim 49 which is covalently modified with a water-soluble polymer.

51. The polypeptide of Claim 50 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol

homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols, and polyvinyl alcohol.

*Jib A8* 52. A composition comprising a nucleic acid molecule of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

53. A composition of Claim 52 wherein said nucleic acid molecule is contained in a viral vector.

*Jib A9* 54. A viral vector comprising a nucleic acid molecule of Claims 1, 2, or 3.

15 55. A fusion polypeptide comprising the polypeptide of Claims 13, 14, or 15 fused to a heterologous amino acid sequence.

20 56. The fusion polypeptide of Claim 55 wherein the heterologous amino acid sequence is an IgG constant domain or a fragment thereof.

*Jib A10* 57. A method for treating, preventing or ameliorating a medical condition comprising administering to a patient the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid of Claims 1, 2, or 3.

30 58. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

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- (a) determining the presence or amount of expression of the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3 in a sample; and
- 5       (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.
- 10      59. A device, comprising:
- (a) a membrane suitable for implantation; and
- (b) cells encapsulated within said membrane, wherein said cells secrete a protein of Claims 13, 14, or 15, and wherein said membrane is permeable to said protein and impermeable to materials detrimental to said cells.
- 15      60. A method of identifying a compound which binds to a polypeptide comprising:
- 20      (a) contacting the polypeptide of Claims 13, 14, or 15 with a compound; and
- (b) determining the extent of binding of the polypeptide to the compound.
- 25      61. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of Claims 1, 2, or 3.

62. A transgenic non-human mammal comprising the nucleic acid molecule of Claims 1, 2, or 3.